

Application No.: 09/674,962  
Inventor: HAUER  
Reply to Office Action of February 27, 2007  
Docket No.: 4904I

### REMARKS/ARGUMENTS

#### Claim Rejections under 35 U.S.C. § 103

Claims 5-9 stand rejected under 35 U.S.C. § 103 (a) as allegedly unpatentable over Volz et al. (*Journal of Chromatography*) in view of Guerinot et al. (U.S. Patent No. 5,846,821) and Haymore et al. (EP 409,814). The Office Action alleges that “it would have been obvious to one having ordinary skill in the art at the time of the invention to pick and choose from the 20 naturally occurring amino acid, the ones that can occupy the x positions in the peptide sequence motif of Volz.” Applicant respectfully traverses the rejection.

The Examiner asserts that Volz et al. describes a peptide fragment of formula HXHXXXCXXC (SEQ ID NO:1) in which Leu is present in the position of the peptide fragment corresponding to X<sup>3</sup>, and any of the 20 naturally-occurring amino acid residues in the positions of the other X variables. The Examiner further asserts the pending claims place Ile where Volz et al. place Leu and that based on teachings of Guerinot et al. and Haymore et al., Leu and Ile can be substituted for each other without losing metal binding properties. None of the pending claims recite peptides containing Ile in X<sup>3</sup> position.

#### Conservative Amino Acid Substitutions Cannot Be Applied to All Substitutions

The Examiner asserts Guerinot et al. (U.S. Patent No. 5,846,821) describes that conservative amino acid residues (e.g. Leu and Ile) can be substituted for one another, especially in non-essential positions. Further, the Examiner relies upon this assertion in an attempt to establish that it would have been obvious to one having ordinary skill in the

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art at the time the invention was made to pick and choose from the 20 naturally occurring amino acids.

Contrary to the Examiner's conclusion that the intervening amino acid residues "X" are non-essential positions, Applicant submits these are "essential" positions supported by Applicant's disclosure at least on page 4, lines 19-26; page 5, lines 23-31; and Example 6 (starting on page 19). The substitution of intervening amino acid residues in these "essential" positions supports the non-obviousness and patentability of Applicant's claimed invention over the prior art.

In arguing the Examiner's general assertion regarding amino acid substitution, Applicant submits that Guerinot et al. specifically states "[a] "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain." (column 14, lines 18-21). Guerinot et al. defines families of amino acid residues having similar side chains; where the family of "non-polar" side chain amino acids is defined to include alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, and tryptophan. (column 14, lines 21-30). Additionally, Guerinot et al. concludes "a predicted nonessential amino acid residue...is preferably replaced with another amino acid residue from the same side chain. (column 14, lines 30-33). While conservative amino acid substitution may have been known to one having ordinary skill in the art at the time of the invention, there is simply no teaching or suggestion for substitutions for different side chain families; simply picking and choosing from the 20 naturally occurring amino acids would not have been obvious.

The Board of Patent Appeals & Interferences decision stated "wherein the only difference between the prior art peptide fragment and the peptide fragment...is a lle

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residue at position X<sup>3</sup> instead of a Leu residue, we agree with the [E]xaminer that it would have been obvious to one of ordinary skill in the art to construct a peptide fragment having the claimed conservative amino acid substitution (i.e., a peptide fragment wherein X<sup>3</sup> is a Leu residue).” (page 5, lines 16-18). In the decision, the Board of Patent Appeals further indicated Guerinot et al. “merely provides evidence of the correctness of the Examiner’s position that these two amino acids are functional equivalents”, referring to Ile and Leu. (page 6, lines 14-15). Applicant submits that absent is any recitation for “non-polar” side chain amino acids for position X<sup>3</sup>, upon which the Examiner is relying for the application of the applied references and which the Board of Appeals decision was based on, are present in claims 5-9. Instead Applicant submits claims 5-9 provide for position X<sup>3</sup> to be the “uncharged polar” side chain amino acids glycine, threonine, tyrosine, and serine. At least according to Guerinot et al., amino acids in “non-polar” and “uncharged polar” families are not regarded as conservative substitutions. (column 14, lines 18-30).

Therefore, the Examiner’s sweeping assertion of the possibility that all 20 naturally occurring amino acid maybe substituted for one another is unfounded and is not supported by either the prior art or the decision by the Board of Patent Appeals & Interferences.

#### The Prior Art Suggests Non-Obviousness & Teaching Away

The Examiner asserts that Haymore et al. (page 4, lines 10-13) confirms the suggestion by Volz et al. that the intervening amino acids denominated as “X” are not critical to the metal binding activity of the peptide. Further, the Examiner asserts that

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Haymore et al. (page 17, lines 14-15) states the intervening residues ("X") are not important. To characterize the teachings of Haymore et al. would be to conclude that at the time of the reference such intervening amino acid residues were not considered critical to metal binding activity. Hence, applying the Examiner's rationale, it would be not be obvious for one of ordinary skill in the art at the time of the invention to substitute any of the intervening amino acids denominated as "X". Indeed, absent from Haymore et al. is a suggestion or motivation to perform any substitutions on intervening residues whatsoever; therefore, the reference fails to support the Examiner's obviousness conclusion.

Further analysis of the teachings of Haymore et al., as directed by the Examiner, lead one of ordinary skill in the art at the time of the invention to conclude the exact opposite. That is, according to Haymore et al., substitution of an intervening amino acid denominated as "X" would result in no change in the metal binding activity of the peptide. Applicant respectfully submits that the prior art, thus, actually suggests that any attempt to substitute an intervening amino acids denominated by "X" would yield no material effect in metal binding and would be futile in nature. Accordingly, there is simply no motivation in Haymore et al. to make such substitution.

Absence of Teaching, Suggestion, and Motivation to Combine Prior Art

While Applicant appreciates that "[t]he obviousness analysis cannot be confined by a formalistic conception of the words teaching, suggestion, and motivation, or by overemphasis on the importance of published articles and the explicit content of issued patents[,]” the U.S. Supreme Court has made clear that an inquiry into whether there was

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“...a teaching, suggestion, or motivation to combine known elements [provides] a helpful insight.” *KSR Int'l v. Teleflex, Inc.*, 550 U.S. \_\_\_\_ (2007). Such an inquiry helps to uphold the well-settled principle that an invention “composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art.” *Id.*

In view of the above, Applicant respectfully submits that the Examiner has attempted to render the instant claims obvious, “merely by demonstrating that each of its elements was, independently, known in the prior art” and by using hindsight reconstruction to use “that which the inventor taught against its teacher.” *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F2d 1540 (Fed Cir 1983). In this regard, Volz et al. (*Journal of Chromatography*), Guerinot et al. (U.S. Patent No. 5,846,821), and Haymore et al. (EP 409,814) do not disclose or suggest to one of ordinary skill in the art a desirability to substitute the claimed intervening amino acid residues in order to affect metal binding activity of the peptide. Guerinot et al. is directed to “conservative” amino acid substitutions (column 14, lines 18-30) of isoleucine with leucine (non-polar side chain), when applied in view of Volz et al. Guerinot et al. does not direct one to substitute non-polar side chain amino acid residues with uncharged polar side chain amino acids, as taught by Applicant. Accordingly, it more appears that the Examiner has used hindsight reconstruction and the Applicant’s disclosure “as a blueprint to reconstruct the claimed invention from the isolated teachings of the prior art,” since the “expressed motivation” to combine is lacking from the individual references and does not appear to emanate from that knowledge generally available to the skilled artisan. *Grain Processing Corp. v. American Maize-Products Co.*, 840 F.2d 902 (Fed. Cir. 1988). Haymore et al. is directed

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to variant peptides having at least one metal-chelating amino acid sequence. However, Applicant submits, Haymore et al. teaches that the modification of intervening amino acid residues ("X") is unimportant (page 3, lines 17-27; and page 4, lines 10-11). Thus, the skilled artisan would not be motivated to make the claimed substitution such that the claimed substitution is nonobvious. Therefore, the possible sources of motivation to combine references: 1) the nature of the problem to be solved; 2) the teachings of the prior art; or 3) the knowledge of persons of ordinary skill in the art, are not satisfied. *In re Rouffet*, 149 F.3d 1350, 1357, 47 USPQ2d 1453, 1457-58 (Fed. Cir. 1998).

Beyond the "teaching, suggestion, and motivation" test for establishing obviousness, the Supreme Court suggested further inquiry regarding: 1) whether the problem is recognized by one of ordinary skill in the art; 2) whether the references applied are obvious to use beyond the primary purpose; 3) whether it would be obvious to try; and 4) whether "common sense" would make the invention apparent. *KSR Int'l v. Teleflex, Inc.*, 550 U.S. \_\_\_\_ (2007). Applying the above considerations to the instant case, it is, first, readily clear that Applicant has identified the problem of increased protein selectivity and simplification of protein purification (page 3, lines 1-7 of the instant application), which problem was not recognized by one of ordinary skill in the art. Second, the primary purpose of the invention of Guerinot et al. is directed to improvements of metal-regulated transporters and uses therefor (e.g. transgenic plants) and does not describe or suggest obvious uses beyond its primary purpose. Third, none of the prior art or the references cited by the Examiner render it "obvious to try" to combine the prior art to create the claimed invention; wherein the prior art teaches not to try (e.g. Guerinot et al. & Haymore et al.). Lastly, "common sense" does not direct the

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skilled artisan to fit the teachings of the prior art together like pieces of a puzzle since the teachings of Haymore et al. indicates amino acid substitutions of intervening amino acid residues ("X") are unimportant and the teachings of Guerinot et al. indicates only "conservative" substitutions of the same side chain family is capable of replacement. The explicit and implicit teachings of the prior art references do not disclose, teach or suggest that substitution of the intervening amino acid residue "X" would be a desirable modification to increase the metal binding activity of the peptide. Further, it is not reasonably apparent that such modification emanates from that knowledge generally available to the skilled artisan or "common sense." [T]here must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *KSR Int'l v. Teleflex, Inc.*, 550 U.S. \_\_\_\_ (2007)

Accordingly, for at least the reasons set forth above, Applicant respectfully submits that Volz et al. (Journal of Chromatography) in view of Guerinot et al. (U.S. Patent No. 5,846,821) and Haymore et al. (EP 409,814) fails to disclose or suggest each and every feature of claims 5-9 as required to support a *prima facie* case of obviousness.

Consequently, the rejection should be withdrawn.

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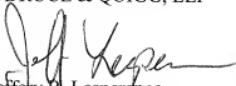
**CONCLUSION**

In view of the foregoing, Applicant respectfully submits that claims 5-9 define subject matter that is patentable over the prior art and is in immediate condition for allowance. Further and favorable reconsideration of this application and the issuance of a Notice of Allowance are requested. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark Office determines that an extension and/or other relief is required, Applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 14-1437. Please credit any excess fees to such deposit account.

Respectfully submitted,

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